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| 10/707,994 | 01/30/2004 | Roger Ariel Alberto | 717859.9 (1292.1) | 1993 |

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| EXAMINER | |
|---|---|
| FETTEROLF, BRANDON J | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 02/26/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/707,994 | ALBERTO ET AL. | |
| | Examiner | Art Unit | |
| | Brandon J. Fetterolf, PhD | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *22-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

***Response to the Amendment***

The Amendment filed on 11/29/2006 in response to the previous Non-Final Office Action (9/18/2006) is acknowledged and has been entered.

Claims 22-42* are currently pending and under consideration.

(*See claim objection below)

**The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.**

**New Objections Necessitated by amendment:**

***Claim Objections***

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not). For example, the amended claims recited two 28 and two 29's.

Misnumbered claims 28-40 have been renumbered 30-42.

**New Rejections Necessitated by amendment:**

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

New claim 32 recites a composition comprising: at least one of an excipients and a diluent; and a compound comprising: a tumor-seeking biomolecules; an intercalating moiety coupled to the tumor-seeking biomolecules and comprising acridine, porphyrin, ellipticine, phenantroline, carbozole, benzimidazole, or a compound that exhibits cytostatic activity; and a metal complexed with the intercalating moiety. However, while the specification teaches that the therapeutic composition comprise at least a suitable amount of a molecule in a diluent or excipients (paragraph 0016) (Emphasis added), the specification and claims, as originally filed, do not appear to have support for the limitation of at least one of an excipients and a diluent. Applicant is invited to point to clear support or specific examples of the claimed limitation in the specification as-filed or remove such amendatory language in response to this action.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

New claims 22-24, 26-29, 32-37 and 40-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Toner et al. (W0 93/21957, 1993, IDS, of record) as evidenced by Albert et al. (US 5,776,894, 1998, of record).

Toner et al. teach a targeting radioactive immunoreagent comprising a metal radionuclide ion, a complexing agent which is a derivative of phenantroline and an immunoreactive group covalently bonded through a protein reactive group to the complexing agent (page 6, lines 1-10 and page 8, lines 9-13, structure A-IV). With regards to the immunoreactive group, the WO document teaches that the immunoreactive group includes, but is not limited to, antibodies such as B72.3, 9.2.27, D612, UJ13A, NRLU-10, 7E11c5, CC49, TNT, PR1A3, ING-1, B174 and B43 antibodies (page 122). With regards to the metal radionuclide ion, the WO document teaches that the radionuclide ion is $^{90}Y$ (page 122). In addition to the disclosure of a targeting radioactive immunoreagent, the WO document teaches a diagnostic composition and a therapeutic composition comprising the radioactive immunoreagent, as well as a method of diagnosing and treating a patient using said radioactive immunoreagent (page 122). Specifically, the WO document teaches that the

radioactive immunoreagent are used for the diagnosis and treatment of a tumor, wherein the immunoreagent is an antibody specific for a tumor antigen (page 61, lines 21-31). Thus, while Toner et al. do not explicitly teach that $^{90}Y$ is a γ emitting nuclide, the claimed limitation does not appear to result in a manipulative difference when compared to the prior arts disclosure in because as evidenced by Albert et al.et al., γ emitting nuclides include, but are not limited to, $^{90}Y$ (column 11, lines 3-8).

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Toner et al. (W0 93/21957, 1993, IDS, of record) in view of Albert et al. (US 5,776,894, 1998, of record).

Toner et al. teach, as applied to claims 22-24, 26-29, 32-37 and 40-42 above, a targeting radioactive immunoreagent comprising a metal radionuclide ion, a complexing agent which is a derivative of phenantroline and an immunoreactive group covalently bonded through a protein reactive group to the complexing agent (page 6, lines 1-10 and page 8, lines 9-13, structure A-IV). With regards to the immunoreactive group, the WO document teaches that the immunoreactive group includes, but is not limited to, antibodies such as B72.3, 9.2.27, D612, UJ13A, NRLU-10, 7E11c5, CC49, TNT, PR1A3, ING-1, B174 and B43 antibodies (page 122). With regards to the metal radionuclide ion, the WO document teaches that the radionuclide ion is $^{90}Y$ (page 122). In addition to the disclosure of a targeting radioactive immunoreagent, the WO document teaches a diagnostic composition and a therapeutic composition comprising the radioactive immunoreagent, as well as a method of diagnosing and treating a patient using said radioactive immunoreagent (page 122). Specifically, the WO document teaches that the radioactive immunoreagent are used for the diagnosis and treatment of a tumor, wherein the immunoreagent is an antibody specific for a tumor antigen (page 61, lines 21-31).

Toner et al. do not explicitly teach that the radioactive metal is selected from the group consisting of Tc-99m, Re-186, Re-188 and Mn.

Albert et al. teach somatostatin peptides bearing at least one chelating group with a detectable element, wherein the detectable elements includes, but is not limited to, g-emitting radionuclides such as Tc-99 and Re-186 (abstract and column 11, lines 3-8). Moreover, Albert et al. teach that the somatostatin peptide bearing at least one chelating group with a detectable element are useful for the visualization and treatment of somatostatin receptor positive tumors (column 12, lines 26-35).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute 90Y as taught by Toner et al. for Tc-99 or Re-186 in view the Albert et al teachings that 90Y, Tc-99 and Re-186 are known γ and β emitters As such, one would have been motivated to do so because Albert et al. teach that 90Y, Tc-99 and Re-186 are each γ and β emitters useful for treatment and visualization of tumors. Thus, one of ordinary skill in the art would have a reasonable expectation that by substituting 90Y as taught by Toner et al. for Tc-99 or Re-186 in view the Albert et al, one would achieve a targeted radioactive immunoreagent for the treatment and diagnosis of a tumor.

Claims 30-31 and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toner et al. (W0 93/21957, 1993, IDS, of record) in view of Holley et al. (Cancer Research 1992; 52: 4190-4195).

Toner et al. teach, as applied to claims 22-24, 26-29, 32-37 and 40-42 above, a targeting radioactive immunoreagent comprising a metal radionuclide ion, a complexing agent which is a derivative of phenantroline and an immunoreactive group covalently bonded through a protein reactive group to the complexing agent (page 6, lines 1-10 and page 8, lines 9-13, structure A-IV). With regards to the immunoreactive group, the WO document teaches that the immunoreactive group includes, but is not limited to, antibodies such as B72.3, 9.2.27, D612, UJ13A, NRLU-10, 7E11c5, CC49, TNT, PR1A3, ING-1, B174 and B43 antibodies (page 122). With regards to the metal radionuclide ion, the WO document teaches that the radionuclide ion is $^{90}Y$ (page 122). In addition to the disclosure of a targeting radioactive immunoreagent, the WO document teaches a diagnostic composition and a therapeutic composition comprising the radioactive immunoreagent,

as well as a method of diagnosing and treating a patient using said radioactive immunoreagent (page 122). Specifically, the WO document teaches that the radioactive immunoreagent are used for the diagnosis and treatment of a tumor, wherein the immunoreagent is an antibody specific for a tumor antigen (page 61, lines 21-31).

Toner et al. do not explicitly teach that tumor seeking molecule is spermidine.

Holley et al. teach a method of targeting chlorambucin to a tumor cell by conjugating chlorambucin to spermidine (page 4191, 1st column, 1st full paragraph). In particular, the reference teaches that the chlorambucin-spermidine conjugate showed greater anti-tumor activity both in vivo and in vitro compared to chlorambucin due to increased tumor uptake and increased affinity for DNA (page 4194, 2nd column, last paragraph)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the conjugate taught by Toner et al. with a spermidine in view of the teachings Holley et al.. One would have been motivated to so because Holley et al. teach that spermidine conjugates show increase tumor uptake and increased affinity for DNA. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by modifying the conjugate taught by Toner et al. with a spermidine in view of the teachings Holley et al, one would achieve a targeted radioactive immunoreagent for the treatment and diagnosis of a tumor.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 22 and 32 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,844,425.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a species anticipates a genus.

The "species" compound comprising: (a) a biomolecule selected from somatostatin, neurotensin, bombesin-receptor binding molecules, antibodies, antennapedia peptide, and molecules binding to GPIIb/GPIIIa receptors; coupled to (b) an aromatic intercalating moiety with binding affinity for double-stranded DNA selected from acridine, porphyrin, ellipticine, phenantroline, carbazole, benzimidazole, and tetracycline compounds with cytostatic activity; which is complexed to (c) a .gamma.-emitting radioactive metal selected from Tc-99m, Re-186, Re-188, and Mn, wherein said compound is associated with one or more pharmaceutically acceptable excipients claimed in the conflicting patent appears to fall within the same scope as the genus of compounds comprising (a) a tumor-seeking biomolecule; coupled to (b) an aromatic intercalating moiety with binding affinity for double-stranded DNA selected from the group consisting of acridine, porphyrin, ellipticine, phenantroline, carbazole, benzimidazole, and tetracycline compounds with cytostatic activity; which is complexed to a metal compound claimed in the instant application being examined.

Therefore, No claim is allowed.

**All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.**

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the

mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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